LIQUID-LIQUID INTERFACE SEGMENT FLOW METHOD AND SEGMENT ANALYSIS METHOD

Publication number: JP2002277478
Publication date: 2002-09-25
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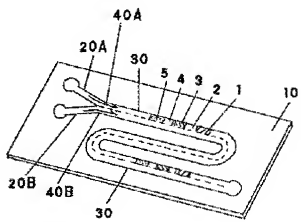
Classification:
- international: ***G01N31/20; G01N21/05; G01N21/41; G01N21/80; G01N35/08; G01N37/00;*** **G01N31/20; G01N21/03; G01N21/41; G01N21/77; G01N35/08; G01N37/00;** (IPC1-7): G01N35/08; G01N21/05; G01N21/41; G01N21/80; G01N31/20; G01N37/00
- European:
Application number: JP20010075086 20010315
Priority number(s): JP20010075086 20010315

Abstract of **JP2002277478**

PROBLEM TO BE SOLVED: To achieve a new technique for further integrating chemical reaction and substance migration, ion analysis, and the like in a micro channel for continuation by accurately controlling flow. SOLUTION: In two taminar flows for forming the interface between liquids in the micro channel (30) on a micro chip (10), at least one solution flow (40A) is composed of several solution segments (1), (2), (3), (4), and (5) having different compositions.



Family list
1 family member for: **JP2002277478**
Derived from 1 application

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IPC: ***G01N31/20; G01N21/05; G01N21/41*** (+15)

Publication info: JP2002277478 A - 2002-09-25

Data supplied from the ***esp@cenet*** database - Worldwide

(19)日本国特許庁（ＪＰ）　(12)公開特許公報（Ａ）　(11)特許出願公開番号
特開2002－277478
（P2002－277478Ａ）
(43)公開日　平成14年９月25日(2002.9.25)

(51)Int.Cl.[7]	識別記号	ＦＩ		テーマコード（参考）
Ｇ０１Ｎ 35/08		Ｇ０１Ｎ 35/08	Ｂ	２Ｇ０４２
21/05		21/05		２Ｇ０５４
21/41		21/41	Ｚ	２Ｇ０５７
21/80		21/80		２Ｇ０５８
31/20		31/20		２Ｇ０５９

審査請求　未請求　請求項の数14　ＯＬ　（全 6 頁）　最終頁に続く

(21)出願番号　特願2001－75086(P2001－75086)

(22)出願日　平成13年３月15日(2001.3.15)

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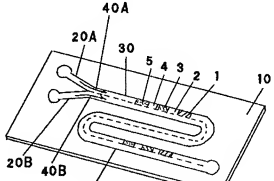
(54)【発明の名称】　被液界面セグメントフロー方法とセグメント分析方法

(57)【要約】
【課題】　より高度な流れの制御によって、マイクロチャンネル内での化学反応や物質移動、イオン分析等をさらに集積化して、連続化することも可能な、新しい技術手段を実現する。
【解決手段】　マイクロチップ（１０）上のマイクロチャンネル（３０）内で液液界面を形成する２層流において、少なくとも一方の溶液流れ（４０Ａ）は、組成の異なる溶液セグメントの複数（１）（２）（３）（４）（５）により構成されているものとする。



【特許請求の範囲】
【請求項１】　マイクロチップ上のマイクロチャンネル内で液液界面を形成する２層流において、少なくとも一方の溶液流れは、組成の異なる溶液セグメントの複数により構成されていることを特徴とする液液界面セグメントフロー方法。
【請求項２】　組成の異なる複数の溶液セグメントの少なくとも一つに、他方の溶液流れに含有されている成分を選択的に抽出分離することを特徴とする請求項１の液液界面セグメントフロー方法。
【請求項３】　組成の異なる複数の溶液セグメントの少なくとも一つと他方の溶液流れとにより選択的液液界面反応を行わせることを特徴とする請求項１の液液界面セグメントフロー方法。
【請求項４】　組成の異なる溶液セグメントは、異なる認識物質を含有していることを特徴とする請求項１ないし３のいずれかの液液界面セグメントフロー方法。
【請求項５】　組成の異なる溶液セグメントは、認識物質を含有しているものと含有していないものとからなることを特徴とする請求項１ないし４のいずれかの液液界面セグメントフロー方法。
【請求項６】　組成の異なる溶液セグメントは、異なる色素を含有していることを特徴とする請求項１ないし５のいずれかの液液界面セグメントフロー方法。
【請求項７】　組成の異なる溶液セグメントは、色素を含有しているものと含有していないものとからなることを特徴とする請求項１ないし６のいずれかの液液界面セグメントフロー方法。
【請求項８】　液液界面を構成する２層流は、一方の溶液流れと他方の溶液流れとの合流域のマイクロチャンネル内において横並行流として形成されることを特徴とする請求項１ないし７のいずれかの液液界面セグメントフロー方法。
【請求項９】　液液界面を構成する２層流は、一方の溶液流れと他方の溶液流れとの合流域のマイクロチャンネル内において上下交差流として形成されることを特徴とする請求項１ないし７のいずれかの液液界面セグメントフロー方法。
【請求項１０】　請求項１ないし９のいずれかの方法により形成された液液界面セグメントフローの少なくとも一方の流れに対し、溶液セグメントに含有される成分の検出を行うことを特徴とするセグメント分析方法。
【請求項１１】　検出を非接触で行うことを特徴とする請求項１０のセグメント分析方法。
【請求項１２】　複数の溶液セグメントの各々に含有されている異なる成分を、溶液セグメント毎に連続して検出することを特徴とする請求項１０または１１のセグメント分析方法。
【請求項１３】　請求項１ないし９のセグメントフロー方法のためのシステムであって、２層流液液界面が形成されるマイクロチャンネルとともに、組成の異なる溶液セグメントの複数より構成される少くとも一方の溶液流れの供給手段とその供給チャンネル並びに他方の溶液流れの供給手段とその供給チャンネルを備えていることを特徴とするセグメントフローシステム。
【請求項１４】　請求項１３のシステムにおいて、検出手段を備えていることを特徴とするセグメント分析システム。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】この出願の発明は、液液界面セグメントフロー方法とセグメント分析方法に関するものである。さらに詳しくは、この出願の発明は、マイクロチップ上において、各種類のイオン等の連続分析や選択的抽出分離等を可能とする、新しい技術としての液液界面セグメントフロー方法とこれを利用したセグメント分析方法、そしてこれらを可能とするセグメントフローシステムに関するものである。
【０００２】
【従来の技術と発明の課題】ガラス板やシリコン基板等のチップ上に数百ミクロン程度までの溝（マイクロチャンネル）を形成し、化学分析や化学反応等をシステムとして集積化することが全世界的に注目を集め、精力的な検討が進められている。
【０００３】しかしながら、これまでの多くは電気泳動分析をチップ上に集積しようとするものであって、一般的な化学反応を集積化するとの試みは数少ないのが実情である。
【０００４】このような状況において、この出願の発明者らは、マイクロチャンネルのような液相微小空間が有するサイズ効果に着目し、これまでに様々な化学反応をマイクロチャンネル内で可能とすることを検討してきた。その結果として、大きな比界面積および短い分子拡散距離に着目してのマイクロチャンネル内での液液抽出法を実現し、極めて有効なイオンセンシング手段であることを確認している。この方法によって、たとえば具体的には、コバルトイオン等の錯形成・溶媒抽出やイオン対検出システムの集積化に成功している。
【０００５】そこで、発明者らは、これまでの実績をさらに発展させ、より高度な流れの制御によって、マイクロチャンネル内での化学反応や物質移動、イオン分析等をさらに集積化して、連続化することも可能な、新しい技術手段を実現することを課題としてきた。
【０００６】
【課題を解決するための手段】この出願の発明は、上記の課題を解決するものとして、第１には、マイクロチップ上のマイクロチャンネル内で液液界面を形成する２層流において、少なくとも一方の溶液流れは、組成の異なる溶液セグメントの複数により構成されていることを特徴とする液液界面セグメントフロー方法を提供する。

【0007】また、第2には、組成の異なる複数の溶液セグメントの少なくとも一つに、他方の溶液流れに含有されている成分を選択的に抽出分離することを特徴とする液液界面セグメントフロー方法を提供し、第3には、組成の異なる複数の溶液セグメントの少なくとも一つと他方の溶液流れとにより選択的液液界面反応を行わせることを特徴とする液液界面セグメントフロー方法を提供する。

【0008】そして、この出願の発明は、上記方法について、第4には、組成の異なる溶液セグメントは、異なる認識物質を含有していることを特徴とする液液界面セグメントフロー方法を、第5には、組成の異なる溶液セグメントは、認識物質を含有しているものと含有していないものとからなることを特徴とする液液界面セグメントフロー方法を、第6には、組成の異なる溶液セグメントは、異なる色素を含有していることを特徴とする液液界面セグメントフロー方法を、第7には、組成の異なる溶液セグメントは、色素を含有しているものと含有していないものとからなることを特徴とする液液界面セグメントフロー方法を提供する。

【0009】この出願の発明は、第8には、液液界面を構成する2層流は、一方の溶液流れと他方の溶液流れとの合流域のマイクロチャンネル内において横並行流として形成されることを特徴とする上記いずれかの液液界面セグメントフロー方法を提供し、第9には、液液界面を構成する2層流は、一方の溶液流れと他方の溶液流れとの合流域のマイクロチャンネル内において上下交差流として形成されることを特徴とする液液界面セグメントフロー方法を提供する。

【0010】さらにこの出願の発明は、第10には、上記いずれかの方法により形成された液液界面セグメントフローの少くとも一方の流れに対し、溶液セグメントに含有される成分の検出を行うことを特徴とするセグメント分析方法を提供し、第11には、検出を非接触で行うことを特徴とするセグメント分析方法を、第12には、複数の溶液セグメントの各々に含有されている異なる成分を、溶液セグメント毎に連続して検出することを特徴とするセグメント分析方法を提供する。

【0011】また、第13には、上記のセグメントフロー方法のためのシステムであって、2層流液液界面が形成されるマイクロチャンネルとともに、組成の異なる溶液セグメントの複数より構成される少くとも一方の溶液流れの供給手段とその供給チャンネル並びに他方の溶液流れの供給手段とその供給チャンネルを備えていることを特徴とするセグメントフローシステムを提供し、第14には、このシステムにおいて、検出手段を備えていることを特徴とするセグメント分析システムを提供する。

【0012】

【発明の実施の形態】この出願の発明は上記のとおりの特徴をもつものであるが、以下に、その実施の形態について説明する。

【0013】添付した図面の図1は、この出願の発明の液液界面セグメントフロー方法の概要を説明したものである。たとえばこの出願の発明は、この図1に例示したようなマイクロチップ（10）において実施される。

【0014】この図1に例示したマイクロチップ（10）は、例えばガラス、シリコン、プラスチック等の透明性のセル基板からなっており、基板の表面は同じく透明性のカバーによって被覆されている。またチップのサイズは縦横の長さが数センチの範囲内に小型化されている。

【0015】このマイクロチップ（10）の基板表面には、2本の微小通液路（20A）（20B）が形成されており、これらが合流してマイクロチャンネル（30）を形成している。微小通液路（20A）（20B）に導入された溶液は、それぞれ図中矢印方法に流れ、マイクロチャンネル（30）内で合流し、2層流液液界面を形成する。この時、2層流となるためには、溶液流れ（40A）（40B）は、互いに非相溶性もしくは難相溶性であって、たとえば一方の溶液流れ（40A）は有機溶液により、他方の溶液流れ（40B）は水溶液により構成される。

【0016】このような液液界面を形成する2層流において、この出願の発明では、たとえば一方の流れとしての有機溶液からなる溶液流れ（40A）を、その組成の異なる溶液セグメント（1）（2）（3）（4）（5）の連続流れとして構成する。組成としては、たとえば、

セグメント（1）：A^+イオノフォア／溶媒
セグメント（2）：溶媒のみ
セグメント（3）：B^+イオノフォア／溶媒
セグメント（4）：溶媒のみ
セグメント（5）：C^+イオノフォア／溶媒

のように構成することができる。もちろん、特定のイオノフォアを含有するものとこれを含有しないものとのセグメントの組合わせに限定されないことは言うまでもない。特有の反応活性分子や、色素等の適宜なものを含有するもの、これらを含有しないもの等のセグメントの組み合わせとして構成してもよい。

【0017】このような溶液セグメントの流れは、前記の微小通液路（20A）に対し、各々の溶液セグメントに対応する供給手段としてのマイクロシリンジ等から、順次に連続するように各々の溶液セグメントを供給することにより形成可能となる。溶液流れ（40A）をどのような溶液セグメントにより構成するかによって、様々な化学反応や抽出、分析等が可能となる。

【0018】たとえば、図2は、上記例示のように、特有のイオノフォアを含有する溶液セグメントの構成によって、他方の溶液流れ（40B）より、特有のイオン種A^+、B^+、C^+を選択的に溶液流れ（40A）のセグメントに抽出して取り込み、その存在を、連続的に検出す

るようにした例を示している。

【００１９】溶液セグメントにより構成される溶液流れ（４０Ａ）については、他方の溶液流れ（４０Ｂ）と、図１および図２に例示したように、マイクロチャンネル（３０）内において横並行流として２層流液液界面を形成してもよいし、あるいは、合流域のマイクロチャンネル（３０）内において、上下流として形成してもよい。上下流においては、比重の問題をも考慮し、液液界面の形成が短時間となるように、流速、流量等を調整してもよいし、あるいは、マイクロチップの構造として、マイクロチャンネルを上下階層構造に形成し、合流域のマイクロチャンネル（３０）は、上下の交差流れとなるようにしてもよい。

【００２０】たとえば以上のような液液界面セグメントフローシステムは、各種の検出手段を備えた分析システムとして構成することができる。たとえば、好適な検出手段としては、この出願の発明者らにより実現されてきた熱レンズ顕微鏡による非接触での分析が可能とされる。合流域マイクロチャンネル（３０）の下流において、たとえば水溶液の溶液流れ（４０Ｂ）からの抽出にともなう溶液流れ（４０Ａ）の各々の溶液セグメントに含有されている複数のイオン種等の各々を検出することが可能となる。

【００２１】熱レンズ顕微鏡によるイオン検出においては、たとえば脂溶性の色素をイオノフォアとともに有機溶液セグメントに含有することが有効でもある。これは、図３にその原理を示したように、分析目的のイオンの検出が、色素分子のプロトン放出によってより高精度に検出可能となるからである。

【００２２】実際、色素溶液の導入による熱レンズ信号の識別性は極めて顕著である。図４は、色素溶液と１－ブタノールのみを交互にセグメントとしてとして導入した場合の熱レンズ信号の強度変化を例示したものである。このことからも識別性の高いことが理解される。

【００２３】もちろん、この出願の発明の液液界面セグメントフロー方法、これを利用した分析方法、並びにこれらの方法を実現するシステムのための具体的手段については、すでに発明者らが提案している様々な態様が採用されてよい。また、実際の溶液セグメントの組成や、マイクロチャンネル内での流量、流速、さらには検出部位、検出手段について適度に定められることは言うまでもない。

【００２４】そこで、以下に実施例を示し、さらに詳しくこの出願の発明について説明する。当然のことであるが、以下の例によって発明が限定されることはない。

【００２５】

【実施例】図２の例において、イオノフォアA*とB*を各々含有する溶液セグメントと、溶媒のみの溶液セグメントとからなる有機相を溶液流れ（４０Ａ）として、イオンの抽出、分析を行った。

【００２６】すなわち、図１および図２に対応して、幅約１５０μｍ、深さ約５０μｍのマイクロチャンネル（３０）に、片方の導入口から、溶液流れ（４０Ｂ）として、Ｎａ*及びK*を１０$^{-2}$Ｍ含む水溶液を導入する。もう一方の導入口からは脂溶性ｐＨ指示薬（ＫＤ－Ａ３）とＮａ*イオノフォア分子（ＤＤ１６Ｃ５）、及びＫＤ－Ａ３とK*イオノフォア分子(Valinomycin) を含む有機相を、イオノフォアを含まない有機相を間にはさむ形の溶液セグメントの構成として、一定の流速及び導入間隔（１μｌ／ｍｉｎ、２ｍｉｎ）でセグメント導入した。溶液流れ（４０Ａ）の有機相と溶液流れ（４０Ｂ）の水相の合流点から距離約１６６ｍｍ下流の有機相側に熱レンズ顕微鏡（励起光波長：５１４．５ｍｍ、プローブ光波長：６３３ｎｍ）の焦点を合わせ、有機相セグメントに抽出されるイオン濃度を測定した。

【００２７】K*イオノフォアを含む有機相セグメント及びＮａ*イオノフォアを含む有機相セグメントを交互に導入したところ、それぞれのセグメントにおいて、特定イオンの選択的抽出に基づく応答が得られた。ここでは１回の連続測定に必要な試薬量が有機相、水相とも約６μｌ程度（試薬量１５０ｐｍｏｌ程度）であり、過渡応答を測定する場合にはさらに試薬量を微量化できる。以上の結果から、１枚のチップ上での多種類イオン連続的検出という、従来型センサーにはないメリットが初めて実現された。このようなシステムはイオノフォアを代えるのみで異なるイオンが測定可能であるため、環境試料、血清試料など、複数イオンの連続分析が要求される分野への適用が可能である。

【００２８】

【発明の効果】以上詳しく説明したとおり、この出願の発明によって、発明者らによるこれまでの実績をさらに発展させ、より高度な流れの制御によって、マイクロチャンネル内での化学反応が物質移動、イオン分析等をさらに集積化して、連続化することも可能な、新しい技術手段が実現される。

【図面の簡単な説明】

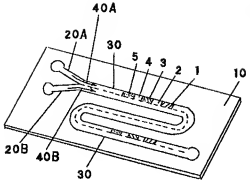
【図１】セグメントフローの概要を示した図である。

【図２】多種類イオンの連続分析システムの概要を示した図である。

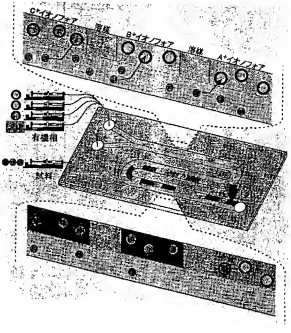
【図３】イオン検出における色素分子の有用性について示した図である。

【図４】色素の有無による熱レンズ信号強度の変化を例示した図である。

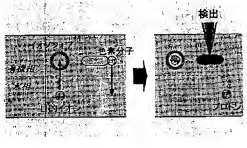
【図1】



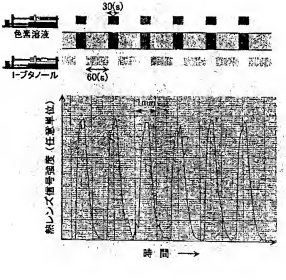
【図2】



【図3】



【図4】



フロントページの続き

(51)Int.Cl.7	識別記号	FI	テーマコード（参考）
G01N 37/00	101	G01N 37/00	101

Fターム(参考) 2G042 AA01 BE05 CB03 DA08 EA03
FA11 HA02
2G054 AA02 CA10 CE10 EA06 FA07
FA28 FA29 FA43 GA03 GB04
2G057 AA05 AA20 AB01 AC01 BA05
BB01 BB02 BB04 BB06
2G058 AA01 AA05 DA09 GA06
2G059 AA03 BB04 CC12 DD03 DD12
DD16 EE11 FF03 HH02 HH06

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CLAIMS

[Claim(s)]
[Claim 1] One [at least] solution flow is the liquid-liquid-interface-level segment flow approach characterized by being constituted by the plurality of the solution segment from which a presentation differs in the two-layer style which forms a liquid liquid interface level within the micro channel on a microchip.
[Claim 2] The liquid-liquid-interface-level segment flow approach of claim 1 characterized by carrying out extraction separation of the component contained with the solution flow of another side to at least one of two or more of the solution segments from which a presentation differs alternatively.
[Claim 3] The liquid-liquid-interface-level segment flow approach of claim 1 characterized by making the solution flow of at least one and another side of two or more solution segments from which a presentation differs perform an alternative liquid-liquid interface reaction.
[Claim 4] The solution segment from which a presentation differs is claim 1 characterized by containing different recognition matter thru/or one liquid-liquid-interface-level segment flow approach of 3.
[Claim 5] The solution segment from which a presentation differs is claim 1 characterized by consisting of a thing containing the recognition matter, and a thing which is not contained thru/or one liquid-liquid-interface-level segment flow approach of 4.
[Claim 6] The solution segment from which a presentation differs is claim 1 characterized by containing different coloring matter thru/or one liquid-liquid-interface-level segment flow approach of 5.
[Claim 7] The solution segment from which a presentation differs is claim 1 characterized by consisting of a thing containing coloring matter, and a thing which is not contained thru/or one liquid-liquid-interface-level segment flow approach of 6.
[Claim 8] The two-layer style which constitutes a liquid liquid interface level is claim 1 characterized by being formed as a horizontal parallel current flow in the micro channel of the entrance region of one solution flow and the solution flow of another side thru/or one liquid-liquid-interface-level segment flow approach of 7.
[Claim 9] The two-layer style which constitutes a liquid liquid interface level is claim 1 characterized by being formed as a vertical crosscurrent in the micro channel of the entrance region of one solution flow and the solution flow of another side thru/or one liquid-liquid-interface-level segment flow approach of 7.
[Claim 10] Segment analytical method characterized by detecting the component contained in a solution segment to one [at least] flow of the liquid-liquid-interface-level segment flow formed by the approach of claim 1 thru/or either of 9.
[Claim 11] Segment analytical method of claim 10 characterized by detecting by non-contact.
[Claim 12] Segment analytical method of claims 10 or 11 characterized by detecting continuously a different component contained to each of two or more solution segments for every solution segment.
[Claim 13] The segment flow system characterized by equipping with the supply means and its supply channel of solution flow of another side one [which consists of plurality of the solution segment from which it is a system for claim 1 thru/or the segment flow approach of 9, and a presentation differs with

the micro channel in which a two-layer flow liquid liquid junction side is formed / at least] supply means and its supply channel list of solution flow.
[Claim 14] The segment analysis system characterized by having the detection means in the system of claim 13.

[Translation done.]

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] Invention of this application relates to the liquid-liquid-interface-level segment flow approach and segment analytical method. Invention of this application relates to the liquid-liquid-interface-level segment flow approach as a new technique and the segment analytical method using this which make possible continuous analysis, alternative extraction separation, etc. of various kinds, such as ion, on a microchip, and the segment flow system which makes these possible in more detail.
[0002]
[The technical problem of a Prior art and invention] The slot (micro channel) to about hundreds of microns is formed on chips, such as a glass plate and a silicon substrate, integrating a chemical analysis, a chemical reaction, etc. as a system attracts attention worldwide, and energetic examination is advanced.
[0003] A few [however, / an attempt that old many tend to accumulate electrophoresis analysis on a chip and a general chemical reaction is integrated / the actual condition]
[0004] In such a situation, the artificers of this application have examined making chemical reactions various until now possible within a micro channel paying attention to the size effect which liquid phase minute space like a micro channel has. the big ratio as the result -- the solvent extraction within the micro channel which pays its attention to an interface product and a short molecular diffusion distance is realized, and it is checking that it is a very effective ion sensing means. Specifically by this approach, it has succeeded, for example in integration of complexing and solvent extraction, such as cobalt ion, and an ion pair detection system.
[0005] Then, artificers developed the old track record further and came considering realizing the new technical means which it integrates further and can also continuation-ize the chemical reaction within a micro channel, mass transfer, ion analysis, etc. by control of more advanced flow as a technical problem.

[0006]
[Means for Solving the Problem] The 1st is provided with the liquid-liquid-interface-level segment flow approach characterized by one [at least] solution flow being constituted by the plurality of the solution segment from which a presentation differs in the two-layer style which forms a liquid liquid interface level within the micro channel on a microchip as that to which invention of this application solves the above-mentioned technical problem.
[0007] Moreover, the 2nd is provided with the liquid-liquid-interface-level segment flow approach characterized by carrying out extraction separation of the component contained with the solution flow of another side to at least one of two or more of the solution segments from which a presentation differs alternatively, and the 3rd is provided with the liquid-liquid-interface-level segment flow approach characterized by making the solution flow of at least one and another side of two or more solution segments from which a presentation differs perform an alternative liquid-liquid interface reaction.
[0008] Invention of this application about the above-mentioned approach and to the 4th The liquid-

liquid-interface-level segment flow approach characterized by the solution segment from which a presentation differs containing different recognition matter to the 5th The liquid-liquid-interface-level segment flow approach characterized by the solution segment from which a presentation differs consisting of a thing containing the recognition matter, and a thing which is not contained to the 6th The liquid-liquid-interface-level segment flow approach characterized by the solution segment from which a presentation differs containing different coloring matter to the 7th The liquid-liquid-interface-level segment flow approach characterized by the solution segment from which a presentation differs consisting of a thing containing coloring matter and a thing which is not contained is offered.

[0009] The two-layer style from which invention of this application constitutes a liquid liquid interface level in the 8th The liquid-liquid-interface-level segment flow approach of one of the above characterized by being formed as a horizontal parallel current flow in the micro channel of the entrance region of one solution flow and the solution flow of another side is offered. The two-layer style which constitutes a liquid liquid interface level provides the 9th with the liquid-liquid-interface-level segment flow approach characterized by being formed as a vertical crosscurrent in the micro channel of the entrance region of one solution flow and the solution flow of another side.

[0010] As opposed to one [at least] flow of the liquid-liquid-interface-level segment flow by which invention of this application was furthermore formed in the 10th by the approach of one of the above The segment analytical method characterized by detecting the component contained in a solution segment is offered. To the 11th The segment analytical method characterized by detecting continuously a different component which contains the segment analytical method characterized by detecting in the 12th at each of two or more solution segments for every solution segment by non-contact is offered.

[0011] With moreover, the micro channel which is a system for the above-mentioned segment flow approach and by which a two-layer flow liquid liquid junction side is formed in the 13th The segment flow system characterized by equipping with the supply means and its supply channel of solution flow of another side one [which consists of plurality of the solution segment from which a presentation differs / at least] supply means and its supply channel list of solution flow is offered. To the 14th In this system, the segment analysis system characterized by having the detection means is offered.

[0012]

[Embodiment of the Invention] Although invention of this application has the description as above-mentioned, it explains the gestalt of that operation below.

[0013] Drawing 1 of the attached drawing explains the outline of the liquid-liquid-interface-level segment flow approach of invention of this application. For example, invention of this application is carried out in a microchip (10) which was illustrated to this drawing 1 .

[0014] The microchip (10) illustrated to this drawing 1 consists of a cel substrate of transparency, such as glass, silicon, and plastics, and, similarly the front face of a substrate is covered with covering of transparency. Moreover, the size of a chip is miniaturized at within the limits whose die length in every direction is several cm.

[0015] Two minute dipping ways (20A) (20B) are formed, these join and the micro channel (30) is formed in the substrate front face of this microchip (10). The solution introduced into the minute dipping way (20A) (20B) flows to the arrow-head approach in drawing, respectively, joins within a micro channel (30), and forms a two-layer flow liquid liquid junction side. In order to become a two-layer style at this time, solution flow (40A) (40B) is immiscible nature or difficulty compatibility mutually, for example, one solution flow (40A) is constituted by the organic solution, and the solution flow (40B) of another side is constituted by the water solution.

[0016] In the two-layer style which forms such a liquid liquid interface level, the solution flow (40A) which consists of an organic solution as flow which is one side, for example consists of invention of this application as continuation flow of the solution segment (1) from which that presentation differs, (2), (3), (4), and (5). As a presentation, only a segment (3):B+ ionophore / solvent segment (4):solvent can constitute only a segment (1):A+ ionophore / solvent segment (2):solvent like a segment (5):C+ ionophore / solvent, for example. Of course, it cannot be overemphasized that it is not limited to the combination of the segment of the thing containing a specific ionophore and the thing which does not

contain this. You may constitute as a combination of segments, such as a characteristic labile molecule, and a thing containing proper things, such as coloring matter, a thing which does not contain these.
[0017] Formation of the flow of such a solution segment is attained from the micro syringe as a supply means corresponding to each solution segment etc. to the aforementioned minute dipping way (20A) by supplying each solution segment so that it may continue one by one. Various chemical reactions, an extract, analysis, etc. are attained by what kind of solution segment constitutes solution flow (40A).
[0018] For example, drawing 2 extracts and incorporates characteristic ion kind A+, B+, and C+ from the solution flow (40B) of another side to the segment of solution flow (40A) alternatively by the configuration of the solution segment containing a characteristic ionophore like the above-mentioned instantiation, and the example which detected the existence continuously is shown.
[0019] About the solution flow (40A) constituted by the solution segment, as illustrated to solution flow (40B), and drawing 1 and drawing 2 of another side, a two-layer flow liquid liquid junction side may be formed as a horizontal parallel current flow in a micro channel (30), or you may form as a vertical style in the micro channel (30) of an entrance region. The rate of flow, a flow rate, etc. may be adjusted, or a micro channel is formed in a vertical layered structure as structure of a microchip, and you may make it the micro channel (30) of an entrance region serve as up-and-down crossover flow also in consideration of the problem of specific gravity, in a vertical style, as formation of a liquid liquid interface level serves as a short time.
[0020] For example, the above liquid-liquid-interface-level segment flow systems can be constituted as an analysis system equipped with various kinds of detection means. For example, as a suitable detection means, analysis non-contact [under the heat lens microscope realized by the artificers of this application] is enabled. In the lower stream of a river of an entrance region micro channel (30), it becomes possible to detect each, such as two or more ion kinds contained in each solution segment of the solution flow (40A) accompanying the extract from the solution flow (40B) of a water solution.
[0021] In the ion detection under a heat lens microscope, it is also effective to contain the coloring matter of lipophilicity in an organic solution segment with an ionophore, for example. This is because the detection of detection of the ion for the purpose of analysis to high degree of accuracy is attained by proton emission of a coloring matter molecule, as the principle was shown in drawing 3 .
[0022] Epicritic [of the heat lens signal by installation of a coloring matter solution] is actually very remarkable. Drawing 4 illustrates a change of the heat lens signal at the time of presupposing by turns that it is only a coloring matter solution and 1-butanol as a segment, and introducing them on the strength. An epicritic high thing is understood also from this.
[0023] Of course, various modes which artificers have already proposed may be adopted about the concrete means for the liquid-liquid-interface-level segment flow approach of invention this application, the analytical method using this, and the system that realizes these approaches in a list. Moreover, it cannot be overemphasized the presentation of an actual solution segment, the flow rate within a micro channel, the rate of flow, and that at least a detecting element is further defined moderately about a detection means.
[0024] Then, an example is shown below and invention of this application is explained to it in more detail. Invention is not limited by the following examples although it is natural.
[0025]
[Example] In the example of drawing 2 , extract of ion and analysis were performed by making into solution flow (40A) the organic phase which consists of a solution segment which contains ionophore A+ and B+ respectively, and a solution segment of only a solvent.
[0026] That is, corresponding to drawing 1 and drawing 2 , the water solution which contains Na+ and K+ 10-2M is introduced into 150 micrometers of ****, and a micro channel (30) with a depth of about 50 micrometers as solution flow (40B) from inlet of one of the two. From another inlet, they are a lipophilicity pH indicator (KD-A3), Na+ ionophore molecule (DD16C5), and KD-A3 and K+ ionophore molecule (Valinomycin). Segment installation was carried out at intervals of the fixed rate of flow and installation (1microl/min, 2min) as a configuration of the solution segment of the form which sandwiches the organic phase which does not contain an ionophore for the included organic phase in

between. The focus of a heat lens microscope (excitation light-wave length: 514.5mm, probe light wave length:633nm) was doubled with the organic phase side of a distance the lower stream of a river of about 166mm from the juncture of the organic phase of solution flow (40A), and the aqueous phase of solution flow (40B), and the ion concentration extracted by the organic phase segment was measured.
[0027] When the organic phase segment containing the organic phase segment and Na+ ionophore containing K+ ionophore was introduced by turns, in each segment, the response based on the alternative extract of specific ion was obtained. Here, an organic phase and the aqueous phase are about [about 6micro] l (amount of reagents 150pmol extent), and when the amount of reagents required for one continuous measurement measures a transient response, it can carry out [minute amount]-izing of the amount of reagents further. From the above result, the merit which is not in a conventional-type sensor called the variety ion continuous detection on the chip of one sheet was realized for the first time. Since ion which is different only by replacing an ionophore with is measurable, an environmental sample, the blood serum sample of such a system, etc. are possible for application in the field as which the continuous analysis of two or more ion is required.
[0028]
[Effect of the Invention] The old track record by artificers is further developed by invention of this application, and a new technical means with it is realized as explained in detail above. [able for the chemical reaction within a micro channel to integrate further, and to continuation-ize mass transfer, ion analysis, etc. by control of more advanced flow,]

[Translation done.]

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TECHNICAL FIELD

[Field of the Invention] Invention of this application relates to the liquid-liquid-interface-level segment flow approach and segment analytical method. Invention of this application relates to the liquid-liquid-interface-level segment flow approach as a new technique and the segment analytical method using this which make possible continuous analysis, alternative extraction separation, etc. of various kinds, such as ion, on a microchip, and the segment flow system which makes these possible in more detail.

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EFFECT OF THE INVENTION

[Effect of the Invention] The old track record by artificers is further developed by invention of this application, and a new technical means with it is realized as explained in detail above. [able for the chemical reaction within a micro channel to integrate further, and to continuation-ize mass transfer, ion analysis, etc. by control of more advanced flow,]

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TECHNICAL PROBLEM

[The technical problem of a Prior art and invention] The slot (micro channel) to about hundreds of microns is formed on chips, such as a glass plate and a silicon substrate, integrating a chemical analysis, a chemical reaction, etc. as a system attracts attention worldwide, and energetic examination is advanced.
[0003] A few [however, / an attempt that old many tend to accumulate electrophoresis analysis on a chip and a general chemical reaction is integrated / the actual condition]
[0004] In such a situation, the artificers of this application have examined making chemical reactions various until now possible within a micro channel paying attention to the size effect which liquid phase minute space like a micro channel has. the big ratio as the result -- the solvent extraction within the micro channel which pays its attention to an interface product and a short molecular diffusion distance is realized, and it is checking that it is a very effective ion sensing means. Specifically by this approach, it has succeeded, for example in integration of complexing and solvent extraction, such as cobalt ion, and an ion pair detection system.
[0005] Then, artificers developed the old track record further and came considering realizing the new technical means which it integrates further and can also continuation-ize the chemical reaction within a micro channel, mass transfer, ion analysis, etc. by control of more advanced flow as a technical problem.

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MEANS

[Means for Solving the Problem] The 1st is provided with the liquid-liquid-interface-level segment flow approach characterized by one [at least] solution flow being constituted by the plurality of the solution segment from which a presentation differs in the two-layer style which forms a liquid liquid interface level within the micro channel on a microchip as that to which invention of this application solves the above-mentioned technical problem.
[0007] Moreover, the 2nd is provided with the liquid-liquid-interface-level segment flow approach characterized by carrying out extraction separation of the component contained with the solution flow of another side to at least one of two or more of the solution segments from which a presentation differs alternatively, and the 3rd is provided with the liquid-liquid-interface-level segment flow approach characterized by making the solution flow of at least one and another side of two or more solution segments from which a presentation differs perform an alternative liquid-liquid interface reaction.
[0008] Invention of this application about the above-mentioned approach and to the 4th The liquid-liquid-interface-level segment flow approach characterized by the solution segment from which a presentation differs containing different recognition matter to the 5th The liquid-liquid-interface-level segment flow approach characterized by the solution segment from which a presentation differs consisting of a thing containing the recognition matter, and a thing which is not contained to the 6th The liquid-liquid-interface-level segment flow approach characterized by the solution segment from which a presentation differs containing different coloring matter to the 7th The liquid-liquid-interface-level segment flow approach characterized by the solution segment from which a presentation differs consisting of a thing containing coloring matter and a thing which is not contained is offered.
[0009] The two-layer style from which invention of this application constitutes a liquid liquid interface level in the 8th The liquid-liquid-interface-level segment flow approach of one of the above characterized by being formed as a horizontal parallel current flow in the micro channel of the entrance region of one solution flow and the solution flow of another side is offered. The two-layer style which constitutes a liquid liquid interface level provides the 9th with the liquid-liquid-interface-level segment flow approach characterized by being formed as a vertical crosscurrent in the micro channel of the entrance region of one solution flow and the solution flow of another side.
[0010] As opposed to one [at least] flow of the liquid-liquid-interface-level segment flow by which invention of this application was furthermore formed in the 10th by the approach of one of the above The segment analytical method characterized by detecting the component contained in a solution segment is offered. To the 11th The segment analytical method characterized by detecting continuously a different component which contains the segment analytical method characterized by detecting in the 12th at each of two or more solution segments for every solution segment by non-contact is offered.
[0011] With moreover, the micro channel which is a system for the above-mentioned segment flow approach and by which a two-layer flow liquid liquid junction side is formed in the 13th The segment flow system characterized by equipping with the supply means and its supply channel of solution flow of another side one [which consists of plurality of the solution segment from which a presentation differs / at least] supply means and its supply channel list of solution flow is offered. To the 14th In this

system, the segment analysis system characterized by having the detection means is offered.
[0012]
[Embodiment of the Invention] Although invention of this application has the description as above-mentioned, it explains the gestalt of that operation below.
[0013] Drawing 1 of the attached drawing explains the outline of the liquid-liquid-interface-level segment flow approach of invention of this application. For example, invention of this application is carried out in a microchip (10) which was illustrated to this drawing 1 .
[0014] The microchip (10) illustrated to this drawing 1 consists of a cel substrate of transparency, such as glass, silicon, and plastics, and, similarly the front face of a substrate is covered with covering of transparency. Moreover, the size of a chip is miniaturized at within the limits whose die length in every direction is several cm.
[0015] Two minute dipping ways (20A) (20B) are formed, these join and the micro channel (30) is formed in the substrate front face of this microchip (10). The solution introduced into the minute dipping way (20A) (20B) flows to the arrow-head approach in drawing, respectively, joins within a micro channel (30), and forms a two-layer flow liquid liquid junction side. In order to become a two-layer style at this time, solution flow (40A) (40B) is immiscible nature or difficulty compatibility mutually, for example, one solution flow (40A) is constituted by the organic solution, and the solution flow (40B) of another side is constituted by the water solution.
[0016] In the two-layer style which forms such a liquid liquid interface level, the solution flow (40A) which consists of an organic solution as flow which is one side, for example consists of invention of this application as continuation flow of the solution segment (1) from which that presentation differs, (2), (3), (4), and (5). As a presentation, only a segment (3):B+ ionophore / solvent segment (4):solvent can constitute only a segment (1):A+ ionophore / solvent segment (2):solvent like a segment (5):C+ ionophore / solvent, for example. Of course, it cannot be overemphasized that it is not limited to the combination of the segment of the thing containing a specific ionophore and the thing which does not contain this. You may constitute as a combination of segments, such as a characteristic labile molecule, and a thing containing proper things, such as coloring matter, a thing which does not contain these.
[0017] Formation of the flow of such a solution segment is attained from the micro syringe as a supply means corresponding to each solution segment etc. to the aforementioned minute dipping way (20A) by supplying each solution segment so that it may continue one by one. Various chemical reactions, an extract, analysis, etc. are attained by what kind of solution segment constitutes solution flow (40A).
[0018] For example, drawing 2 extracts and incorporates characteristic ion kind A+, B+, and C+ from the solution flow (40B) of another side to the segment of solution flow (40A) alternatively by the configuration of the solution segment containing a characteristic ionophore like the above-mentioned instantiation, and the example which detected the existence continuously is shown.
[0019] About the solution flow (40A) constituted by the solution segment, as illustrated to solution flow (40B), and drawing 1 and drawing 2 of another side, a two-layer flow liquid liquid junction side may be formed as a horizontal parallel current flow in a micro channel (30), or you may form as a vertical style in the micro channel (30) of an entrance region. The rate of flow, a flow rate, etc. may be adjusted, or a micro channel is formed in a vertical layered structure as structure of a microchip, and you may make it the micro channel (30) of an entrance region serve as up-and-down crossover flow also in consideration of the problem of specific gravity, in a vertical style, as formation of a liquid liquid interface level serves as a short time.
[0020] For example, the above liquid-liquid-interface-level segment flow systems can be constituted as an analysis system equipped with various kinds of detection means. For example, as a suitable detection means, analysis non-contact [under the heat lens microscope realized by the artificers of this application] is enabled. In the lower stream of a river of an entrance region micro channel (30), it becomes possible to detect each, such as two or more ion kinds contained in each solution segment of the solution flow (40A) accompanying the extract from the solution flow (40B) of a water solution.
[0021] In the ion detection under a heat lens microscope, it is also effective to contain the coloring matter of lipophilicity in an organic solution segment with an ionophore, for example. This is because

the detection of detection of the ion for the purpose of analysis to high degree of accuracy is attained by proton emission of a coloring matter molecule, as the principle was shown in drawing 3 .
[0022] Epicritic [of the heat lens signal by installation of a coloring matter solution] is actually very remarkable. Drawing 4 illustrates a change of the heat lens signal at the time of presupposing by turns that it is only a coloring matter solution and 1-butanol as a segment, and introducing them on the strength. An epicritic high thing is understood also from this.
[0023] Of course, various modes which artificers have already proposed may be adopted about the concrete means for the liquid-liquid-interface-level segment flow approach of invention this application, the analytical method using this, and the system that realizes these approaches in a list. Moreover, it cannot be overemphasized the presentation of an actual solution segment, the flow rate within a micro channel, the rate of flow, and that at least a detecting element is further defined moderately about a detection means.
[0024] Then, an example is shown below and invention of this application is explained to it in more detail. Invention is not limited by the following examples although it is natural.

[Translation done.]

* NOTICES *

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EXAMPLE

[Example] In the example of drawing 2 , extract of ion and analysis were performed by making into solution flow (40A) the organic phase which consists of a solution segment which contains ionophore A+ and B+ respectively, and a solution segment of only a solvent.
[0026] That is, corresponding to drawing 1 and drawing 2 , the water solution which contains Na+ and K+ 10-2M is introduced into 150 micrometers of ****, and a micro channel (30) with a depth of about 50 micrometers as solution flow (40B) from inlet of one of the two. From another inlet, they are a lipophilicity pH indicator (KD-A3), Na+ ionophore molecule (DD16C5), and KD-A3 and K+ ionophore molecule (Valinomycin). Segment installation was carried out at intervals of the fixed rate of flow and installation (1microl/min, 2min) as a configuration of the solution segment of the form which sandwiches the organic phase which does not contain an ionophore for the included organic phase in between. The focus of a heat lens microscope (excitation light-wave length: 514.5mm, probe light wave length:633nm) was doubled with the organic phase side of a distance the lower stream of a river of about 166mm from the juncture of the organic phase of solution flow (40A), and the aqueous phase of solution flow (40B), and the ion concentration extracted by the organic phase segment was measured.
[0027] When the organic phase segment containing the organic phase segment and Na+ ionophore containing K+ ionophore was introduced by turns, in each segment, the response based on the alternative extract of specific ion was obtained. Here, an organic phase and the aqueous phase are about [about 6micro] l (amount of reagents 150pmol extent), and when the amount of reagents required for one continuous measurement measures a transient response, it can carry out [minute amount]-izing of the amount of reagents further. From the above result, the merit which is not in a conventional-type sensor called the variety ion continuous detection on the chip of one sheet was realized for the first time. Since ion which is different only by replacing an ionophore with is measurable, an environmental sample, the blood serum sample of such a system, etc. are possible for application in the field as which the continuous analysis of two or more ion is required.

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DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]
[Drawing 1] It is drawing having shown the outline of a segment flow.
[Drawing 2] It is drawing having shown the outline of the continuous analysis system of variety ion.
[Drawing 3] It is drawing having shown the usefulness of the coloring matter molecule in ion detection.
[Drawing 4] It is drawing which illustrated change of the heat lens signal strength by the existence of coloring matter.

[Translation done.]

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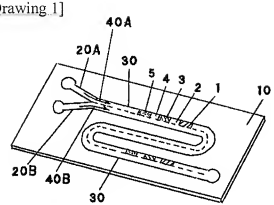
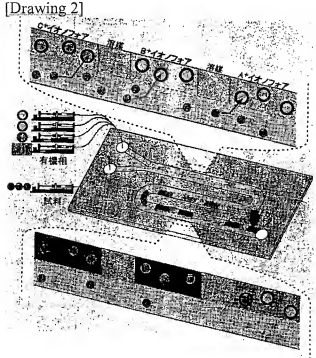
DRAWINGS

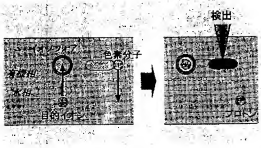
[Drawing 1]



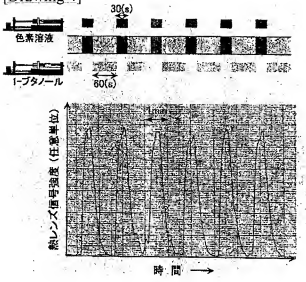
[Drawing 2]



[Drawing 3]



[Drawing 4]



[Translation done.]